Stony Brook University (NY, USA) has recently announced that Professor of Biomedical Engineering, Danny Bluestein, has received a US$7.5 million Phase II Quantum grant from the US NIH; this is the first time that a professor from Stony Brook has received this grant. The goal of the project is the assessment and improvement of various cardiovascular (CVS) devices, with the ultimate goal of eliminating the requirement for anticoagulation with these devices.

“...an array of CVS devices from various manufacturers will be tested and optimized, with the ultimate goal to reduce their thrombogenicity...”

While the millions of CVS prosthetic devices implanted worldwide save many lives, they promote the formation of blood clots, necessitating the administration of anticoagulants; however, this can result in dangerous bleeding due to the coagulation suppression. If the requirement for anticoagulation could be removed from these devices, it could lead to a very large reduction in these bleeding events and could facilitate a significant improvement in long-term use of such devices; Bluestein has discussed these important concepts previously in an editorial for the Expert Review of Medical Devices.

Outlining the problems with existing circulatory support technology, Bluestein said, “Over 5 million patients in the USA suffer annually from heart failure, with their number expected to grow by 50% over the next 15 years. Of those, a significant proportion will become candidates for longer-term mechanical circulatory support. While the advent of CVS devices has provided life-saving solutions to these patients, thromboembolism and the attendant risk for cardioembolic stroke remains an impediment for mechanical circulatory support devices. The mandatory life-long anticoagulant drug regimen required to mitigate this problem induces vulnerability to hemorrhage, is not a viable therapy for certain populations of patients and does not eliminate this risk. It is still the critical barrier to their use for long-term destination therapy.”

The Phase II grant will allow Bluestein to carry on the important work conducted during Phase I of the Quantum project. In this phase of the project, Bluestein and his colleagues used laboratory models to develop and test a novel technology designed to reduce the need for anticoagulation therapy with implantable CVS devices; he commented, “In our Phase I of the Quantum project, which was funded under a special high-risk/high-impact applications program, a thrombogenicity predictive technology – Device Thrombogenicity Emulator (DTE) – was successfully developed and its application to design optimization for achieving improved thrombogenic performance in CVS devices was demonstrated.” Discussing Phase II of the project, Bluestein said, “In this Quantum Phase II project that was awarded to us, an array of CVS devices from various manufacturers will be tested and optimized, with the ultimate goal to reduce their thrombogenicity to a level that will liberate the device recipients from the need for complex pharmacological anticoagulation therapy ... During Phase II of our Quantum project, the DTE will be utilized to optimize the design of various subgroups of CVS devices: prosthetic heart valves (PHV), ventricular assist devices (VAD), and the first US FDA-approved temporary total artificial heart (TAHt). All these devices generate very complex pathological flow fields, implicated in their elevated thrombogenicity, thus offering a real challenge for optimizing their thrombogenic performance. The DTE uses stress-loading waveforms, extracted from detailed numerical flow modeling in the devices, that are programmed into a computer-controlled hemodynamic shearing device (HSD) capable of emulating device hemodynamics with great accuracy, where the resultant thrombogenicity is measured using an innovative platelet activity state (PAS) assay. The DTE methodology is used to optimize the thrombogenic performance of the devices by facilitating the testing of virtual device design modifications before prototypes are built and tested in costly preclinical and clinical trials.”

The DTE technology is utilized to generate highly detailed flow models of CVS devices, which are used to identify areas within a device that are susceptible to blood clot formation. The design can then be optimized to reduce the requirement for anticoagulation.

Bluestein elaborated on the DTE methodology, stating:

- “Detailed numerical modeling of the flow field through each device is performed. Those include several PHV (mechanical, polymeric and bioprosthetic), pulsatile and rotary VAD, and TAHt. The models include highly resolved 3D-device geometries for studying small-scale flow phenomena in regions leading to thromboembolism. Sophisticated turbulence and fluid–structure interaction models with advanced material properties, as well as direct numerical simulations are employed.
- Design specific ‘hot spot’ regions that may lead to device thrombogenicity during distinct flow phases are identified, and flow trajectories within these regions
that expose platelets to elevated stresses and lead them towards activation are computed. The spatial–temporal stress distribution along the pertaining trajectories are then extracted as stress-loading waveforms.

• Various design parameters of PHV, VAD and TAHt implicated in device thrombogenicity are numerically studied and iteratively optimized for reducing the thrombogenic potential of the devices. The optimization is conducted in an iterative process. The resultant trajectories of the optimized designs are then extracted as stress-loading waveforms.

• The HSD emulates the device and design-specific flow conditions. In it, blood platelets are uniformly exposed to the dynamic loading waveforms extracted from the ‘hot spot’ trajectories of the numerical simulations and programmed into the HSD, then compared to those after optimization. Their resultant activity is measured using an innovative, highly sensitive PAS assay, capable of sensitive measurements of flow-induced platelet hemostatic activity in devices.

The DTE methodology is used for optimizing the design modifications aimed at reducing the thrombogenicity to a level that will eliminate the need for anticoagulants in the following manner: the loading waveforms of the optimized designs are programmed into the HSD for testing, and the resulting platelet activity and thrombogenicity is measured to establish whether it was reduced to a level that does not require anticoagulation. Once such reduction is achieved, prototypes of the optimized designs are constructed by the device manufacturers participating in our Quantum project. The optimization is tested by us in vitro to ascertain whether the expected level of nonthrombogenicity was achieved, as assessed in bulk PAS measurements performed in the optimized devices prototypes. This is followed by the optimized prototypes tested by the manufacturers in vivo in preclinical and clinical trials. The participating device manufacturers will seek from the FDA premarket approval/investigational device exemption/humanitarian device exemption, as required, for the type of device and the modifications needed owing to the optimization process.”

Bluestein and his colleagues are optimistic that, by the end of this Quantum II project, some of the CVS devices involved will have reached late-stage preclinical development or early clinical testing without the need for anticoagulation therapy. Bluestein outlined the potential implications and benefits that the DTE technology could bring to the field of CVS devices, “The technology offered will become an essential tool for manufacturers that seek to create, redesign and test a CVS device. Besides reducing research and development costs, it may prevent unfortunate situations where devices need to be recalled or clinical trials stopped because of unacceptable thrombogenicity levels – situations that could be catastrophic to patients and with devastating financial costs to society and device manufacturers alike. These savings will be passed on to patients and will help in drastically reducing the escalating healthcare costs involved. By reducing and ultimately eliminating the need for difficult and costly pharmacological management with anticoagulants, it is expected that it will pave the way for the use of these devices as long-term destination therapy.”


Large-scale trial demonstrates comparable safety profiles between drug-eluting and bare-metal stents

A study published recently in the New England Journal of Medicine has demonstrated that the safety of drug-eluting stents (DESs) is equivalent to the safety of bare-metal stents (BMSs), with a reduced incidence of target vessel revascularization. These promising results contribute to the growing body of safety data on these devices.

The results, presented at the American Heart Association 2010 Scientific Sessions and published on the same day, were designed as a response to a retrospective analysis entitled the Basel Stent Kosten Effektivitäts Trial – Late Thrombotic Events (BASKET-LATE), which raised concerns that after discontinuation of poststent implantation antiplatelet therapy, patients treated with DESs suffered a higher rate of stent thrombosis compared with BMS patients.

The Basel Stent Kosten Effektivitäts Trial – Prosp ectiv e Validation Examination (BASKET-PROVE) trials enrolled 2314 patients requiring a coronary stent 3.0 mm or larger to a first- or second-generation DES, or a BMS. Patients were followed for 24 months following implantation. According to lead investigator Christoph Kaiser, the results demonstrate that “in contemporaneous stenting of large coronary arteries, late safety problems with DESs could not be confirmed and there was even a trend in the opposite direction.”

The primary end point was met, with statistically similar rates of composite death from cardiac causes or nonfatal myocardial infarction at 2 years in first- and second-generation DES and BMS patients.

First successful removal of salivary stone using robotics

The first successful removal of a salivary stone utilizing a surgical robot has been reported by Rohan Walvekar, Director of Clinical Research and the Salivary Endoscopy Service at Louisiana State University Health Sciences Center, New Orleans (LA, USA).

Walvekar used the surgical robot, guided by a miniature surgical endoscope, to successfully remove a 20-mm salivary stone and repair the salivary duct in a 31-year-old patient. Most stones are less than 8 mm in size; traditional methods for removing large stones involve removing the salivary gland completely. This new technique helps preserve the salivary gland and reduce blood loss, scarring and time spent in hospital.

Salivary stones, which can result from the crystallization of salts in the saliva, can lead to a blockage in the duct, leading to swelling, pain and a risk of infection. The combination of salivary endoscopes and the robotic unit has improved surgical view and dexterity in confined spaces, vastly improving the successful removal of stones without removing the duct altogether.

“With these newer advances … we can offer minimally invasive, gland preserving, same-day surgical procedures that represent a tremendous advance over the traditional gland removing surgery,” concluded Walvekar.


Study finds device could reduce difficulty in swallowing in Parkinson’s disease patients

In research published in Neurology, scientists have found that a hand-held device that strengthens the muscles involved in swallowing can reduce a swallowing-associated health risk in Parkinson’s disease (PD) patients. In their article, the authors state that, “Dysphagia is the main cause of aspiration pneumonia and death in PD, with no established restorative behavioral treatment to date.” Michelle Troche (University of Florida, FL, USA) commented, “The many muscles involved in swallowing progressively weaken in patients with PD and become uncoordinated in the same way that patients lose coordination and strength in their arms and legs.” Patients can also find it increasingly difficult to detect material in their airways, and therefore cough with enough force to remove it.

The study was a randomized, blinded, sham-controlled trial of patients with PD. Study participants exhaled into an expiratory muscle-strength training (EMST) device. Christine Sapienza (University of Florida) explained, “EMST uses the basic exercise theory behind any strength training program. This small device capitalizes on that concept of overload with a calibrated pressure release valve that won’t open until you generate a great enough lung pressure … It acts much like a pin on a weight machine and uses the same concept to strengthen the muscles involved in swallowing and breathing.”

In the investigation, one group of participants used a properly calibrated EMST device, whilst another group used a sham device. The devices were used for 20 min/day at home, 5 days/week, for a total of 4 weeks. Swallowing function of the patients was measured pre- and post-treatment using the Penetration–Aspiration scale. Videofluoroscopy was used to achieve ‘motion x-ray images’ of the muscle involved in swallowing when the patients drank liquid. One result demonstrated that 14% of patients in the sham-device group and approximately a third of patients in the calibrated-device group obtained improved swallow safety scores.

“…a hand-held device that strengthens the muscles involved in swallowing can reduce a swallowing-associated health risk in Parkinson’s disease patients.”

Stephanie Daniels (Baylor College of Medicine, Houston, TX, USA) commented, “The fact that EMST is a home-based treatment is of particular importance as many individuals with PD cannot travel the long distance to attend clinic or hospital therapy sessions. Very few swallowing treatment studies have incorporated the rigorous research design used in this study. We need more studies such as this to support the different treatment approaches used in swallowing rehabilitation”. The study authors concluded, “EMST may be a restorative treatment for dysphagia in those with PD.”


About the News in Brief

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